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Fabrication of passive Lab-in-a-Foil devices for phaseguiding and stoichiometric reactions

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Filling larger volumes of fluids and precise mixing is desired for on-chip biochemical reactions to enable further analysis of the sample. In this paper, we present the fabrication and operation of a chip for multiple displacement amplification (MDA) of DNA, where the volume of the amplification product has to be >100 nL for later off-chip analysis.

In recent work, MDA of DNA has been performed on a microfluidic device containing the active push-up valve [1]. We present a fast and cheap fabrication protocol of passive Lab-in-a-Foil devices by using hot embossing. Nevertheless, imprinting large protrusions in the fabrication of large chambers in a polymer device is not trivial, likewise the following experiment where fluid filling of the chamber has to be performed, where a high risk of encapsulating bubbles of air that might block the fluidic device is present [2]. Furthermore, the MDA protocol is a stoichiometric reaction where monitoring and measuring volumes of different reagents is very important. The polymer device consists of a micro fluidic channel, the bus, connecting three inlets to a waste reservoir. The different reagents in the stoichiometric reaction will be added sequentially to the reaction chamber from three inlets by a pressure-driven flow by a fluid-flow towards the waste reservoir by exchanging the reagent in the bus. Each device consists of four reaction chambers parallel connected to the bus by nanoslits with the height of 500 nm. The design overview can be seen in Figure 1. The filling of the empty (air) reactions chamber was controlled in order to monitor and control the stoichiometry of the reaction by designing an array of pillars as showed in Figure 1, and in Figure 2 where a SEM image of a single pillar with the radius and height of 10 μm is shown. The pillars facilitate a preferred flow-direction due to the minimizing of the surface tension.

By the use of the Compact Nanoimprint tool, CNI, from NIL Technology, Denmark, a fast respond-able thermal cycle was possible and enabling high temperatures without drastically increasing the cooling time. The fabrication of the polymer devices in Figure 1 was a four-step fabrication. A three leveled 4" silicon stamp with 10 μm and 500 nm protrusions was fabricated followed by a imprint into TOPAS® 6013 Cyclic Olefin Copolymer (COC) foil heated to 190 °C and a pressure of 6 bar applied on the top of the stack in 20 min. Afterwards a lid of a TOPAS® 6013 was flattened between two anti-stiction coated 4" silicon likewise heated to 190 °C. Finally, the lid and the structured sheet was thermal bonded at 121°C and a pressure of 6 bar applied on the top of the stack. The stacks in the three embossing steps were cooled to 90 °C after embossing. The total fabrication time – device imprint, lid flattening and wafer bonding - of a wafer containing four devices was 90 min.

The outlined principle of phaseguiding will only guide the front of the fluid where a two-dimensional flow in-between the pillars are allowed in the bulk of the fluid. The diffusion length will thereby not be drastically increased, as it is the case if walls were inserted. Furthermore, the pillars are preventing the lid to collapse to the bottom of the chamber and adding another functionality compared to the phaseguiding presented in [2]. Figure 3 shows a sequence of images of the phaseguiding of MilliQ water added 0.01 % Triton-X100 in order to lower the hydrophobic behavior of Topas and thereby lowering the adsorption of DNA which in the MDA protocol would be unwanted [3].

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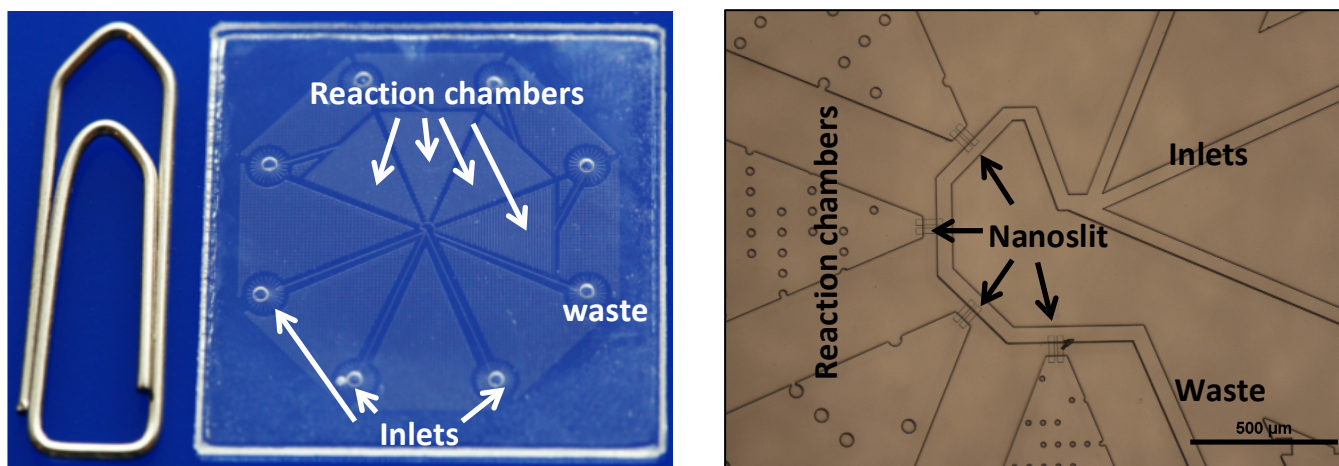


Figure 1. Left: Image showing the final chip with the dimension of 2.5 x 2.5 cm. The chip contains of a micro fluidic channel connecting three inlets and a waste reservoir and four separated reaction chambers are connected to the microchannel by nanoslits of the height of 500 nm where the microstructures are at high of 10 μm . Right: Microscope image showing a zoom of the center of the polymer chip.

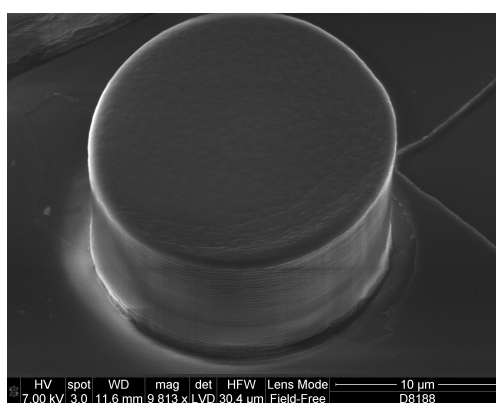


Figure 2. SEM image of an imprinted polymer pillar with a radius and height of 10 μm . The pillar has two functionalities; Supporting the lid and thereby avoid collapse and guiding the filling of the chamber.

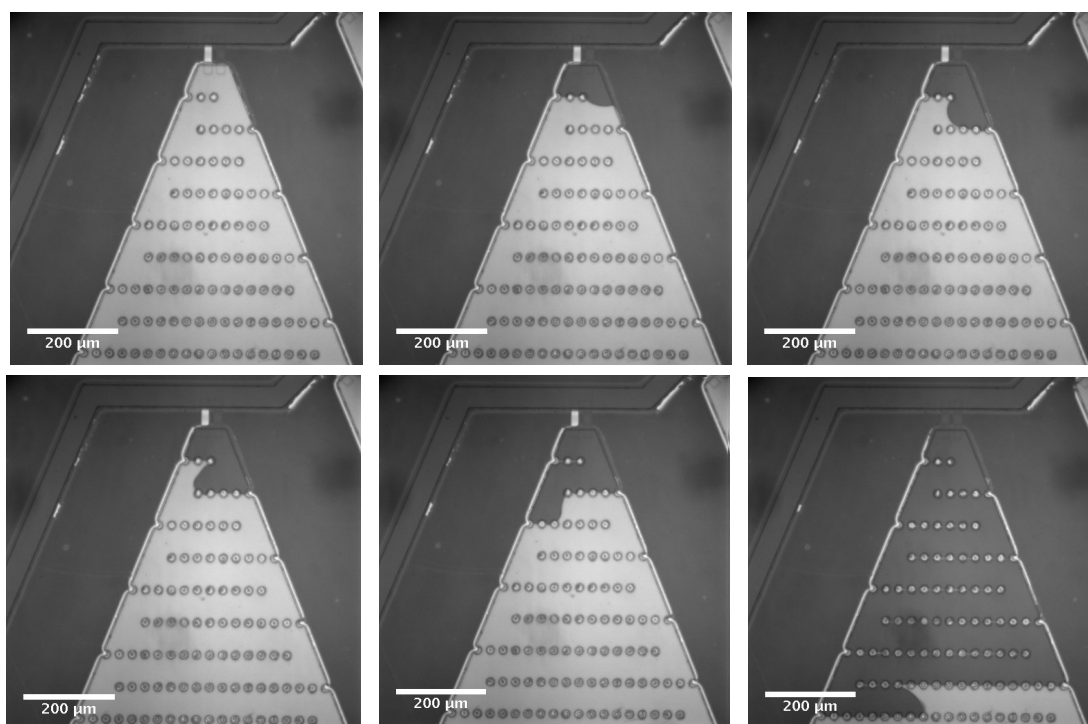


Figure 3. Sequence of microscope images showing the principle of phaseguiding. The array of pillars facilitates a preferred flow-direction. By removing pillars on each row of pillars bursting from one row to the next is specified in the design. The filling showed in the sequence is performed on 30 s.